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THE MILROY LECTURES ON KALA-AZAR, ITS DIFFERENTIATION AND ITS EPIDEMIOLOGY

L. Rogers

Lecture II - Kala-Azar as a Disease.

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IN TWO VOLUMES ANNUALLY.

VOL. I. FOR 1907.

EIGHTY-FIFTH YEAR.

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on the cortical centres renders it easy to understand that it should sometimes excite an epileptic seizure in those who are liable; indeed, we may feel surprise that the effect is so seldom met with. A sudden alarm occasionally induces a true faint, but the alarm is usually more profound than that caused by a sudden sound, and the attack comes on deliberately.

Sudden change of posture is an occasional excitant of loss of consciousness, and it may be regarded as evidence that this is syncopal if the change is to the erect posture. For the moment the flow of blood to the head must be hindered, but in some cases of undoubted epilepsy it may induce an attack. I had once an opportunity of observing such an attack. Consciousness was instantly lost; the patient became rigid and would have fallen unless supported; the conjunctival and pupillary reflexes were absolutely lost. Had it been syncope the onset would have been deliberate, preceded by pallor, and there would have been no rigidity. The mechanism of an epileptic attack thus induced is an interesting problem. The facts suggest the possibility that the sudden diminution in blood pressure, trifling as it must have been, may have caused the nerve elements to pass into the condition which underlies the unconsciousness of a complete syncopal faint. They again bring before us the question whether this may not be identical with that of epilepsy.

Stooping, lowering the head, has the opposite effect on the intracranial circulation; it tends to increase the amount of blood in the vessels, especially when combined with flexion of the neck, hindering the return by the veins, and with some effort, which is usually the object of the stoop. The fulness of the vessels thus induced seems sometimes to cause a momentary loss of consciousness, but this is not alone effective often enough to come into relation to our present subject. A more intense mechanical congestion is induced by severe paroxysms of cough, such as those of whooping-cough. They may culminate in a moment's unconsciousness, as if the sudden increase of blood pressure produced the same functional state of the nerve elements as its sudden decrease. I may mention an interesting personal observation by one of the most distinguished physicians of the last century who had an attack of whooping-cough when nearly 60 years of age. In many of the more severe paroxysms of coughing he had a moment's loss of consciousness. The impression his own sensation gave him was distinctly that this was not the effect of the mechanical congestion; it seemed to him to be due to a process of discharge spreading from that in the medulla which caused the cough.

To the case in which epileptic attacks were induced by standing up the following presents an instructive contrast:—

CASE 7.—A woman, aged 38 years, had epileptic attacks in the night, apparently of minor character but attended by micturition. They also occurred in the day and then began with a sensation of a sudden rush to the head, followed by loss of sight and then loss of consciousness. Automatic action followed the attack. One was so sudden in onset that she fell unconscious on the floor. Thus there can be no question of their epileptic nature. In her, stooping often induced a partial attack, there was a sudden rush to the head, and complete loss of sight, which gradually returned on rising, but there was not actual unconsciousness. Otherwise these attacks, induced by stooping, resembled closely those that were spontaneous. The lesson of the case is that repletion of the vessels and increased intracranial pressure excited the state of the nerve elements which constituted the epileptic seizure. The effect, moreover, bore some resemblance to partial syncope due to cardiac failure, but was more rapid in its course.

The connexion between the cases we have considered is the fact of loss of consciousness. If we realise that the state of the cerebral nerve elements on which it depends may be similar in both syncope and epilepsy, many of the facts of the cases I have referred to become more intelligible. In epilepsy the instability of the nerve elements causes them to pass, suddenly and spontaneously, into the same state as is induced more slowly by the failure of the pressure and flow of blood which result from cardiac syncope. We can then understand that such repeated induction of this state by failure of the heart may lessen their inherent stability, until the change may occur spontaneously as definite minor epilepsy. We can also understand that a change of position which lessens slightly the blood pressure may promote the onset of an attack of epileptic unconsciousness in those who are liable to this.

My chief object is to impress on you the fact that the functional state of the brain in syncopal unconsciousness is distinct from the failure of the blood-supply that causes it, and may be nearly the same as that which occurs in epilepsy, apart from the state of the circulation. Other objects are to direct attention to the uncertainty there is as to the precise mechanism through which the heart failure is induced by its various causes, the occasional causal relation of syncope to epilepsy, the problems of their diagnosis. Perhaps the first object I have just mentioned may now seem superfluous. The definite distinctness of the cerebral process may appear self-evident and it may seem that I have laboured overmuch to make clear that which needs no demonstrating. If so, I am well content.

ABSTRACT OF

The Milroy Lectures

ON

KALA-AZAR, ITS DIFFERENTIATION AND ITS EPIDEMIOLOGY.

Delivered before the Royal College of Physicians of London

BY LEONARD ROGERS, M.D. LOND., F.R.C.P. LOND.,

MAJOR, I.M.S.; PROFESSOR OF PATHOLOGY AT THE MEDICAL COLLEGE, CALCUTTA.

LECTURE II.[1]

Delivered on Feb. 26th.

KALA-AZAR AS A DISEASE.

MR. PRESIDENT AND GENTLEMEN,—In my first lecture I dealt with kala-azar as an epidemic, tracing its origin, spread, and decline, and referred to a similar earlier outbreak in Bengal known as "Burdwan fever." To-day I pass on to describe the disease itself, its course, complications, and terminations, and shall show you that it is not one whit less terrible when considered individually than collectively, for it literally kills by inches after most prolonged sufferings, which we are still powerless to check to any great extent. As the latter stages of the disease are much better known than the earlier ones it will be clearer if I first describe the typical advanced condition, returning to the still rarely recognised commencement of the fever.

[With regard to the general appearances in the characteristic stages of the disease kala-azar, a number of lantern slides showing groups of cases were shown and the salient points of each were described, the main features being the marked contrast between the tumid bellies due to the very great enlargement of the spleens and sometimes also of the liver, contrasting with the great wasting of the chest, face, and limbs. Brief notes were given of a group of hospital cases which illustrated the different courses that disease might take, while a village group showed the great frequency of the affection in children, just as in malarial fever, the incidence decreasing steadily in the subsequent decades. Other groups of sporadic cases, then known as "malarial cachexia," in the Sylhet Valley, which was not invaded by the epidemic, showed the clinical identity of the two forms of the disease, which was the principal argument of the lecturer in his 1897 report in favour of the epidemic disease in the Brahmaputra Valley being but an intensified form of malarial fever. The extreme wasting in the last stages and the occasional dropsical ascitic complication produced by a peculiar form of intracellular cirrhosis of the liver were also illustrated. The lecturer then proceeded:]

Family distribution.—Several of the cases already referred to illustrate very well the extraordinary tendency of this disease to attack a number of persons in the same family or household, but the frequency with which this is the case will be better realised from the following figures relating to 20 successive Assamese patients seen in the Nowgong Hospital. Among their near relatives no less than 123 persons had been attacked by kala-azar, only two of whom recovered from it, while but 44 had escaped the infection, or, to put it

[1] Lecture I. was published in THE LANCET of Feb. 23rd, 1907, p. 486.

another way, no less than four-fifths of these patients had lost half, or more than half, of their relatives within from three to five years, so that it is easy to understand how whole families have been destroyed and so much land has fallen out of cultivation.

A similar family incidence is seen in the sporadic disease and is best illustrated by a European series of cases, in which it is easier to follow up the histories. An examination of my notes of the Calcutta European Hospital cases of the last six years shows that the most common relationships between patients actually in hospital for the disease were parent and child in six instances and brothers and sisters in seven more, nearly always children, while in no less than three of these instances more than two children of the same household were admitted, the series in one family extending over a period of five years. Moreover, just one-third of the whole series of cases had relatives actually in hospital during this period, while a good many more gave histories of other members of their families being attacked with fevers of long duration, which were pretty certainly mostly of the same nature. This family incidence clearly points to a house infection and was the basis of the successful measures which I advocated against the disease.

The histories of the rare cases in which Europeans in Assam were attacked by kala-azar throw some further light on this question, for in all the six cases, regarding whom Mr. J. Dodds Price kindly furnished me with information, the affected men were in the habit of cohabiting with native women either in the infected lines or in three instances with one woman, who was subsequently found to be infected with kala-azar, two of them subsequently dying from the disease. Two of these last cases of infection were most important, as they occurred in parts then uninfected with kala-azar, but in each case the woman had come from an infected district. Moreover, Mr. Price knows of no instance in which a European cohabited with an infected native woman who escaped kala-azar; and when we bear in mind that it is the usual custom for such women only to come to the bungalow at night and not to eat with the European, then it becomes clear that the most likely mode of infection by a parasite occurring in the peripheral circulation is through some biting insect, in which the parasite may pass its extracorporeal stage of existence. Moreover, such a source of infection may furnish a clue to that of adult Europeans with no family history to explain it in large towns such as Calcutta, as well as among soldiers in Bengal cantonments, and is also in accordance with the increasing age incidence after early adult life to be mentioned immediately. Again, the infection of one child after another in the same house may be also readily explained on the same hypothesis, and indicates the importance of isolating, at least in a separate room, any person attacked by the disease, or better is a hospital where persistent treatment and nursing can be carried out.

Age and sex incidence.—Among tea-garden coolies, who furnish the most accurate statistics, there was no difference in the incidence of the disease on the two sexes, nor did occupation affect it. Numberless instances of husband and wife being infected one after the other were met with, it being, in fact, the exception for one of them to escape: another striking instance of house infection. In the sporadic disease in Calcutta an excess of native males are admitted, much in proportion to those of other diseases. In the European hospital there were twice as many males as females above the age of 15 years, possibly partly due to the source of infection just mentioned, but in children under 15 years of age there were 23 females to 13 males, probably due to a larger proportion of the male children living away from home at schools.

The *age incidence* is of great importance, the most striking fact being the number of children attacked. In my report I recorded that 25·6 per cent. of my cases occurred in children under 10 years of age, while 24·4 per cent. more were between 10 and 20 years old, making 50 per cent. under the latter age. Further, in a more recent report on the sporadic disease in Sylhet, 39 per cent. were under 10 years and 30 per cent. more between 10 and and 20 years, making nearly 70 per cent. under 20 years. Among natives in Calcutta only 8 per cent. were in children under 10 years, but 40 per cent. were between 10 and 20 years, three-fifths of which were boys from 10 to 15 years old, who are much more readily brought to hospital than girls or younger children. Between from 20 to 30 years of age there were 32 per cent., 16 per cent. from 30 to 40 years, and only 4 per cent. over 40 years. Among Europeans, who readily bring their children to hospital, 20 per cent. were under 10 years and 22 per cent. more between 10 and 15 years, making no less than 42 per cent. 15 years of age or under, 22 per cent. from 20 to 30 years, and 20 per cent. over 30 years, showing once more a very high rate among the unfortunate children and a decreasing one with advancing age.

Race incidence.—It has already been mentioned that epidemic kala-azar was rare in Europeans in Assam compared with natives, but is not so very uncommon in Europeans in Calcutta in the sporadic form. The class of Europeans attacked is here of great importance, for out of 87 cases, regarding whom I have a note as to how long they had been in India, I find that no less than 87·34 per cent. were born and bred in that country and only 12·66 were immigrants from Europe. Moreover, the shortest time after arriving in India that any immigrant was attacked was eight years, a second had been 13 years, and a third 19 years in the country, while the remaining eight had all been over 20 years in India and belonged to the same class as those born in Calcutta, and, like them, were living in parts of the city where their houses were surrounded by those of native inhabitants and under conditions of overcrowding and bad sanitation. In fact, almost all these unfortunate people belonged to the poorest sections of the mixed European and native population, among whom the sanitation and cleanliness of the well-to-do official and commercial European immigrant class are an impossibility, a fact of great importance in connexion with the etiology of the disease. In marked contrast with this is an observation that I have recently made to the effect that 80 per cent. of the European immigrants admitted to hospital for typhoid fever in Calcutta had been three years or less in India, for the totally different incidence of sporadic kala-azar just mentioned in this class will prove a useful point in the differentiation of the latter disease in its early remittent stage from typhoid fever, with which it has been so much confused.

SEASONAL INCIDENCE OF KALA-AZAR.

Owing to the disease lasting from a few months to several years cases are admitted to hospital at all seasons and neither in Calcutta nor Madras is there any very marked seasonal incidence, although there is some excess of admissions of Europeans in Calcutta at the end of the cold and beginning of the hot season, especially among those coming in the early stages of the fever. Of much greater importance is the question whether the fever begins at any special season, as is suggested by the fact that the extracorporeal stages of the parasite, to be described later, only developed in my cultures below a temperature of 75° F. It is very difficult to obtain accurate histories of the beginning of the disease in many cases, especially when they are seen for the first time at a much later date, but an analysis of my notes of those patients who stated that they had had fever for not more than six months in two series of cases, in the Native Medical College and European hospitals respectively, both showed a marked preponderance commencing during the cold weather or early in the hot weather on account of the frequent long incubation period. These results can be summed up by saying that in the six months from November to April there were three times as many cases in the European series and almost four times as many in the native one as in the remaining six months of the year, a sufficiently striking fact when the difficulties of getting accurate data are considered. When in Assam I tried to work out this point from the admissions to hospital for fever on tea estates and found that most of the patients suffering from typical kala-azar in the cold season had been admitted for short attacks of apparently malarial fever in the previous rainy season from June to October. On finding that the sporadic cases in Calcutta mostly began in the cold season I wrote to Mr. Price for his matured experience on the subject and he very kindly sent me histories of all his European cases, every one of which had commenced in the cold weather, while an inquiry into his then comparatively few native patients also showed that almost all of them had developed kala-azar during the cold weather and he added: "All this is very instructive and fits in exactly with your Calcutta experience."

Taking everything into consideration I think there is sufficient evidence to prove that the great majority of patients become infected in the cold season, and I am inclined to think that infection will ultimately be found to be limited to this time of the year. The importance of this fact in connexion with prophylactic measures is clear, as it

will greatly simplify matters if precautions against infection have only to be taken during a few months of the year.

THE TYPES OF FEVER IN KALA-AZAR.

I now come to the difficult subject of the diagnostic value of the types of fever in kala-azar, my conclusions being based on four-hour temperature charts of every case in the European Calcutta Hospital for several years, and a still larger series in native patients, while as I also possess complete notes and charts of every fever case in the open wards of the European Hospital for two years, I am now in a position to point out the most important features in the diagnosis of kala-azar in the difficult early stages from other fevers with which they are commonly confused. The antern slides prepared from the charts, some of which represent the temperature curves for several months, will best serve to illustrate the types met with.

[The principal points illustrated by the charts shown were the following. The very long duration of the fever, which shows alternating remittent and intermittent types for many months at a stretch, even in the case of patients admitted in a markedly cachectic and anæmic condition, showing the great resisting powers of his patients. When the temperature is of the remittent type there are rapid wasting and impoverishment of the blood, but when it falls to the low intermittent type both the weight and the blood show steady improvement, while quinine in large doses has a marked effect in reducing the high dangerous type of fever to the low comparatively harmless one which may eventually wear itself out and cease entirely, and then the weight is soon regained, and once the patient has been free from fever for two or three months and fully regained the normal weight relapses do not occur and recovery is permanent and complete. Such cessation of the fever and cure sometimes follow a severe septic complication, such as cancrum oris, and are then accompanied by a marked rise in the previously very low number of polynuclear leucocytes, which the lecturer has also been able to produce with good results in a few cases by injections of sterilised cultures of staphylococci, in accordance with the methods of Sir A. E. Wright, although this treatment has not been invariably successful. The good effect of large doses of quinine was illustrated by a nine months chart of a child, aged eight years, seen early in the disease, and whose fever was only finally broken when 50 grains of quinine had been taken daily for seven weeks, her weight also steadily rising from the time this large dose was given, no ill effect being produced by it. The recognition of the fever of kala-azar in its early stage, which usually begins with a high remittent form of pyrexia, may often be accomplished by noting certain peculiarities in four-hour temperature charts. The most important of these, which was illustrated by several slides, is what the lecturer has already described as the double remittent type—namely, a marked daily double or triple rise of the temperature, often for several days together, in the absence of any treatment by the more powerful sweat-producing antipyretic drugs such as antipyrin. This double type is most frequently seen in the earlier periods of the fever, but may occur at any time in its course, and may also occasionally appear during continued or intermittent pyrexia in kala-azar. The great importance of this type is that, in the lecturer's experience, it has never been seen in typhoid fever, for which the early stage of sporadic kala-azar is so frequently mistaken, as in some of the cases illustrated, and this type is almost diagnostic of the new fever, the first case in a European in Bombay having been first suspected on account of the double remissions taking place. Another type of fever shown in the lantern slides, which is rather characteristic of this fever, is a low continued type of pyrexia, the temperature falling below 101°F., but not varying more than 2° in the 24 hours; a type which is much rarer in typhoid fever, in which the pulse is also usually slower than in kala-azar in proportion to the degree of the pyrexia. Moreover, even when the fever is high for long periods in kala-azar there is a characteristic absence of severe distress or typhoid symptoms, patients often saying that they feel quite well and do not think they have any fever, when the thermometer registers 103° or 104°. Once more, when the remittent temperature falls it commonly assumes a low intermittent type, rising to about 100° every afternoon, instead of running a subnormal course as after typhoid fever, a feature that will often allow of the more serious kala-azar being suspected at an early date before the cachectic stage has been reached. A consideration of these various types will nearly always allow of the sporadic affection being suspected at an early date, when persistent treatment is most likely to be of avail, while the blood changes will allow of the diagnosis being confirmed.]

THE SPLEEN AND LIVER IN KALA-AZAR.

Time will not allow of my giving a full clinical account of this remarkable disease (although I hope to do so shortly in a work on Fevers in India, for which I have been collecting material for a number of years), but a few more of the salient points must be touched on.

The spleen.—The great degree of enlargement of the spleen can best be indicated by the following data. In 70 typical advanced cases of the epidemic disease in Assam of which I have notes the spleen was enlarged in all, while in 94·5 per cent. it reached to at least three inches below the costal margin, in 56·5 per cent. it extended to the navel or beyond, while in 27·7 per cent. to the level of the anterior superior spine of the ilium. In 95 consecutive sporadic cases in the Medical College, Calcutta, all verified by finding the parasite in the spleen blood, in 80 per cent. the organ reached to the navel or beyond and in 10 per cent. to the anterior superior spine of the ilium. In a series of earlier sporadic cases at the European General Hospital the spleen extended to the navel or beyond in 63 per cent., being nearly always of this size in cases of over three months duration, although the edge was above the navel in three-fifths of the cases with under one month's history of fever. On the other hand, among 200 healthy coolies I examined in Assam on a tea garden when unaffected with kala-azar I found only 1 per cent. with spleens reaching down to the navel, in only 6 per cent. did it extend three inches below the ribs, while in a total of 25 per cent. the organ could be felt below the ribs—figures which suffice to disprove Dr. G. M. Giles's statement that it would be absurd to attach any importance to enlargement of the spleen in kala azar in such a malarious country as Assam.

The liver.—This organ was enlarged in 93 per cent. of my Assam series, in 75 per cent. of the Medical College, and in 59 per cent. of the European cases in Calcutta, who came earlier under observation, it having been normal in seven-eighths of these European patients admitted during the first month of the fever. The enlargement of the liver to any marked degree is very uncommon in the earlier stages, although after some months it may occasionally reach down to the navel and may then be even larger than the spleen, and eventually become cirrhosed, causing ascites.

The blood changes.—I have elsewhere described the blood changes in kala-azar and pointed out their great value in differentiating it from other diseases, especially fevers, so need only now summarise them. In the first place, an increase in the percentage of the large mononuclear leucocytes is very common and of great value as a point in the differentiation of the early stages of sporadic kala-azar from typhoid fever, for in the latter the lymphocytes, but very rarely the large mononuclears, are increased during the pyrexia. On the other hand, this change is of no help in distinguishing kala-azar from true chronic malaria, in which a large mononuclear increase is also commonly present. These two last diseases may, however, be distinguished by counting the total red and white corpuscles and working out the proportion between the two, for in malaria both are about equally reduced, so that the ratio of white to red remains normal—namely, about 1 to 750—and very rarely, if ever, falls below 1 to 1000, while in kala-azar it is the rule for the white corpuscles to be disproportionately reduced, so that the ratio of white to red is, in the absence of any leucocyte-increasing complication, commonly below 1 to 1500, and not rarely as low as 1 to 2000, 3000, or more. This extraordinary reduction of the leucocytes, which not rarely number but from 500 to 1000 per cubic millimetre, is almost diagnostic of kala-azar, as I have never met them in any other fever cases out of several scores in which I have done blood counts, and it has often enabled me to diagnose the disease in a comparatively early stage. So much is this the case that I now rarely employ the spleen puncture as a diagnostic measure, several fatal cases in addition to those published having come to my knowledge. It should never be done in very anæmic patients or in those who have suffered from any form of hæmorrhage unless the blood is first proved to be clotting normally, while I always take the further precaution of keeping up digital pressure for several minutes after withdrawing the needle and immediately administering a dose of calcium chloride by the mouth. With these precautions it may be of value in some difficult comparatively

early cases in which the confirmation of the diagnosis is of great importance in order to allow of continued and adequate treatment being strongly urged on the patient, so many of whom leave hospital during a temporary remission of their fever and leave off the all-important quinine until a fresh high remittent bout comes to reduce them another stage towards the grave.

COMPLICATIONS OF KALA-AZAR.

The frequency with which kala-azar is terminated by some inflammatory complication may best be illustrated by the data from 40 necropsies made by me at the Medical College Hospital. All but seven of them showed some serious local disease, and some of them more than one. In 11 pneumonia, in ten dysentery, in seven cancrum oris, in two each pneumococcic meningitis, purpura, cerebral hæmorrhage, and pulmonary phthisis respectively, and in one pericarditis were found, while in several cancrum oris cases staphylococci or streptococci were cultivated from the spleen, revealing a general septic infection. The extreme reduction in the polynuclear leucocytes in this disease, in which they not rarely fall to one-twentieth or less of the normal numbers, easily explains the frequency with which these patients fall victims to the specific organisms of pneumonia, dysentery, pulmonary phthisis, or the cocci of cancrum oris in which I have never been able to find the diphtheria bacillus, which has been met with in European cases of this disease.

Hæmorrhages deserve special mention among the complications, reduced coagulability having been found by me in some of these cases, while bleeding from sloughing ulcers or from the stomach or bowel has also been seen, in addition to several cases of bleeding into the brain or its membranes.

THE TREATMENT OF KALA-AZAR.

Although much has been done to elucidate the pathology of kala-azar during the last four years, unfortunately the treatment of the disease has made no corresponding progress and is still in a most unsatisfactory state. In Madras, indeed, I am informed that almost every case is believed to die, the mortality being estimated at 98 per cent., the highest figure reached in the Nowgong tea estates by the epidemic form, while that of several hundred cases treated by Mr. Price at the height of the epidemic gave an average mortality of 96 per cent. Mr. Price's cases were treated with thymol first to exclude ankylostomiasis, and quinine in moderate doses being generally used during the several periods the patients were in hospital, for it was the common opinion that quinine failed to check the fever in the same way that it did malaria, and many thought it quite valueless and used it very little, as is also the case in Madras at the present time. In my report I strongly dissented from this view and urged that quinine did have a definite effect in controlling the severity of the fever, even when it did not stop it altogether, and recommended that it should be given in large doses and persisted with for months together if necessary. Further experience in Calcutta has only served to confirm me in that opinion, for I have repeatedly seen a high remittent fever reduced to a comparatively harmless low intermittent one by increasing the quantity of quinine given, 60 and in some cases 90 grains a day having been taken for considerable periods with nothing but good effects beyond being sometimes distressing to the patients. Once the temperature has fallen to the low intermittent type it can often be kept down to that point for a long time by smaller doses, one of 20 grains in the morning being commonly effectual. That this line of treatment has given far better results than those admitted by unbelievers in it will be clear from the fact that after the publication of my report Mr. Price systematically tried persevering quinine treatment, and when he worked out for me the results of several years' experience he found that the mortality of 500 consecutive cases was but 75 per cent., the remaining 25 per cent. having permanently recovered against 4 per cent. in the earlier series quoted above. Now as these patients were indentured coolies, who remained working on the gardens, often for years, after getting over a typical attack of kala-azar (the diagnosis of which in its characteristic stages presents no difficulties at the present time to Mr. Price with his 15 years' daily experience of the disease, while in some of them the parasite was also found by spleen puncture), there can be absolutely no doubt about their permanent recovery, some of them having also been seen by me both during and after their attacks.

Moreover, these unquestionable results of Mr. Price are confirmed by my smaller experience in Calcutta, under less favourable conditions for following up my patients. Thus, out of 65 cases in the European hospital, during the last three years of which I have notes, 18 who left the hospital in a doubtful condition I have not been able to get further news of, leaving 47 cases. Of these 47 cases 21 died either in hospital or after leaving it, 9 more who left in a worse condition than they came may be counted as having died, leaving 7, or 14·88, who left hospital after having lost their fever and greatly improved, a fair proportion of them probably recovering, and 10, or 21·27 per cent., have completely recovered and are known to have been well for from several months to upwards of a year after leaving hospital. It should be mentioned that three of the patients who recovered had also been treated with injections of staphylococcus vaccine, which appeared to have some good effect.

These figures are in close accordance with those of Mr. Price and contrast most favourably with the nearly invariably fatal results admitted by those who still deny their patients the benefit of persistent quinine treatment, although without any efficient remedy of their own, and I venture to think that in view of the above data my line of treatment should never be neglected until we have a better one to replace it, as I hope and expect will be the case in time. Bone-marrow in tabloids, to repair the blood deterioration, is also of considerable value; arsenic is worthy of trial, while in the form of atoxyl, which is now being advocated in the allied protozoal disease, sleeping sickness, my friend, Captain J. W. D. Megaw, I.M.S., has injected in two cases with at least temporary good effects. Colonel C. P. Lukis, I.M.S., Principal of the Medical College, Calcutta, has also tried cinnimate of soda to increase the leucocytes, but without accomplishing the desired result or doing any good, while x rays over the spleen have been tried by the same observer, but without effecting any cures. In view of the chronicity of the disease and the occasional remarkable spontaneous recoveries from an apparently hopeless state much caution is required in making deductions regarding any line of treatment, but the extraordinary cures which do occur encourage the hope that a better treatment, even than the quinine one, will be found to rescue these unfortunates from the lingering death which still awaits the great majority of them.

THE DISTRIBUTION OF SPORADIC KALA-AZAR IN INDIA.

Since it became known that so many cases previously classed as "malarial cachexia" are but the sporadic form of kala-azar observations on its distribution have been accumulating. Donovan and others have found it to be very common in Madras, while my own observations have shown it to be widely distributed all over Lower Bengal and Assam, except the eastern part of the Brahmaputra valley, while it also occurs somewhat less frequently in Western Bengal or Bihar, and extends into the neighbouring eastern end of the United Provinces of Agra and Oudh, cases in soldiers having been verified by the officers of the Royal Army Medical Corps at Benares, while I have also seen two soldiers who appear to have contracted the disease in Allahabad, and others have been met with among Gurkhas in as far west as Dehra Dun. On the other hand, during an examination of the records of all the fever cases admitted to the Lahore Medical College Hospital for three years I failed to find any cases resembling sporadic kala-azar, while it is also specially noteworthy that I met with no double remittent, low continued, or other doubtful long fevers among them. The Bombay records also show a similar absence of the disease, except rare importations from Madras, so that the disease appears to be limited to the eastern side of India, although I am informed that Burma, like Bombay, only has cases contracted at Madras.

In connexion with this distribution it is of interest to note that the areas affected all have a very mild cold season, during which the mean temperature for three or four months remains between from 60° to 75° F., for I shall show in my concluding lecture that these are the limits between which I have been able to cultivate the parasite outside the human body. On the other hand, in the unaffected north-west parts of India the mean temperature during the cold months falls below 60°, while owing to the brevity of spring and autumn in India the temperature conditions most favourable to the organism outside the human body is a very short one in those areas.

EFFECTS OF SEASONAL VARIATIONS ON THE PREVALENCE AND ORIGIN OF THE DISEASE.

I have already shown that the infection of kala-azar is probably limited to the cold season, so an exceptionally long spell of cold weather might be expected temporarily to increase

the occurrence of the disease. This is actually so, for two years ago such a cold season occurred in Bengal, and during it and the following early hot weather months an unusually large number of sporadic kala-azar cases were admitted to both the native and European hospitals of Calcutta, many more than in the following year with a normal cold season. Now this long spell of cold weather followed an early cessation of the previous monsoon rains, for the withdrawal of the south-west monsoon is succeeded by a cold north breeze, and it will be remembered that in my first lecture I pointed out that the Assam epidemic arose as a consequence of four out of five successive years of deficient rainfall in the early "seventies," due to an early cessation of the monsoon current. I have not been able to get complete meteorological data for the Rungpore district in the "seventies," but those of Calcutta of that period show that during several of the years of deficient rain the mean temperatures of the ensuing cold season were below the average. Now, if a single cold year had such a marked influence in increasing the sporadic kala-azar in Calcutta, on account of the longer period which was favourable to the infection, it becomes easy to understand how an unusual succession of such seasons might have increased the number of cases, and so the foci of infection, year by year, until the fever became so widespread that the people began to leave their villages and thus carried the infection into areas at the foot of the Garo hills and in the Goalpara subdivision, which had hitherto been almost or quite free from it, and so started the spreading the disease in Assam in a people who were extremely susceptible to it owing to not having previously suffered from the sporadic form. Such an origin of the Assam epidemic of kala-azar is most in accordance with the known facts of its history, and also with the life-history of the parasite and mode of infection, which I shall deal with in my remaining lecture.

ABSTRACT OF

The Morison Lectures

ON

INSANITY, WITH SPECIAL REFERENCE TO PROGNOSIS.

Delivered before the Royal College of Physicians of Edinburgh on Jan. 28th and 30th and Feb. 1st, 1907,

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LECTURE I.[1]

Delivered on Jan. 28th.

IN no kind of disease is prognosis more doubtful than in insanity. For long overshadowed by ignorance and superstition, for long regarded as a mysterious calamity, for long obscured by confusing issues, it is only of late years that the fundamental truths have been disengaged from the fantastic phenomena which formerly dominated the attention of the observer. The long-drawn melancholy, the violent excitement, the bizarre ideas, and the dangerous conduct of the insane wholly occupied attention and precluded the study of obscure and elusive bodily conditions. The tedious recital of aberrant talk and morbid conduct long detained us with mere irrelevancies. It is unnecessary to discuss the history of medical literature dealing with insanity, until the memorable publication of Schroeder van der Kolk's lectures on Mental Diseases, which took shape about the middle of last century. He arrived at the conclusion that much insanity is due to morbid conditions of the great intestine. In accordance with the medical ideas of his time he described this class of cases as "sympathetic insanity." While he clearly recognised the brain as the organ of mind, he believed that it is liable to disturbance in direct consequence of somatic conditions, influencing it in a secondary manner. This conclusion was widely supported, and here in Edinburgh the influence of the body on the mind was definitely fixed and crystallised by Skae's classification of mental diseases.

It is almost impossible to gain any useful information from old asylum records. In the earliest series the recorders note the reception of a lunatic and briefly indicate that he was furious or fatuous, sometimes adding an account of heroic doses of medicaments, blistering, and bleeding, and sometimes an indication of removal by death or otherwise. At a later period the cases are described as psychological curiosities—how they arrived on foot or in a carriage, how they displayed their morbid ideas, how they wrote, and how they behaved. But withal the most chary record of physical disorders, the most elusive statements as to family or personal history—in brief, it was the study of mind apart from body—the psychological content. Having arrived at the conclusion that there is no pathology of insanity comment on somatic conditions was, of course, superfluous.

The blood of the insane is the *dernier cri* of the modern investigator. Dr. Lauder Lindsay, so long ago as 1854, published a series of observations on the histology of the blood of the insane, which he had made in the Crichton Royal Institution. He did not claim that his researches elucidated the morbid conditions of mind, or its organ, the brain; but rather illustrated the laws of pathology, the natural relations of healthy and morbid states of mind and body, and more particularly the reaction of physical diseases on mental phenomena. The *résumé* was presented under 14 headings, the fourth being to the effect that a leucocythæmic condition frequently exists. As examples of this, cases of general paralysis, acute mania, and melancholia are cited. Unfortunately, Dr. Lindsay concluded that there was no connexion between the state of the blood and the mental condition, but that it bore a relation to the physical disorder, debilitated conditions of the system, and general vitiation of the blood.

Thirty years elapsed before another systematic investigation of the blood of the insane was undertaken, when Dr. S. R. Macphail in 1884 won the medal of the Medico-Psychological Association. By that time the hæmocytometer and the hæmoglobinometer had been invented and with these instruments of precision further advance was recorded. In general paralysis Dr. Macphail recorded an increase in the relative proportion of white to red corpuscles, coincident with the progress of the disease; he failed to find any great influence on the proportion of white to red corpuscles in maniacal attacks, while in a series of recent admissions the proportion was increased. Most important is his conclusion that there is a close connexion between gain in weight, improvement in the quality of the blood, and mental recovery.

Another prize essay on the same subject was the work of Dr. Johnson Smyth in 1890. He inferred that the relative proportions of white to red corpuscles were so variable as to be of little importance. In many instances, however, he recorded an excess of leucocytes and stated that the blood of the insane is in a pathological condition.

Quite recently the position has been still further developed by the researches and conclusions of yesterday. Within the last few months Dr. L. C. Bruce has published his records of clinical investigations. Much of his book is concerned with observations on the blood of the insane, and specially on the leucocytosis which he has shown to be of definite importance in diagnosis and prognosis. What was dimly discerned by Dr. Lauder Lindsay half a century ago is made clear by Dr. Bruce to-day, and especially the important conclusion that the morbid state of the blood is a dominating factor in the evolution of mental diseases. Sufficient has been said to indicate the growth of medical opinion relevant to insanity as an affair of medicine. Similar references might be made to other somatic conditions the true nature of which is only now intelligible and explicable. I have referred to Schroeder van der Kolk as one of the first to appreciate the toxic nature of insanity. He said: "It is evident that the brain, as the organ through which the higher intellectual powers are immediately manifested, must especially suffer in insanity. We should, however, be much in error in seeking the proper source and cause of the disease always in the brain, for the influence which many organs exercise upon the brain is evident enough." The Hippocratic doctrine that insanity is caused by disease had been obliterated by the superstition of the Middle Ages. The brain, as the organ of mind, infinitely complex in its own proper connexions, is at present the subject of study relative to its relations with all pathological somatic conditions. Thus the sympathetic insanity of van der Kolk is regarded as a term

[1] The lectures were illustrated by statistical tables, charts, and clinical observations.